(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
08 October 2020 (08.10.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/205559 A1

(51) International Patent Classification:
C12M 1/00 (2006.01) *C12M 1/26* (2006.01)

(21) International Application Number:
PCT/US2020/025334

(22) International Filing Date:
27 March 2020 (27.03.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/827,504 01 April 2019 (01.04.2019) US
62/899,829 13 September 2019 (13.09.2019) US

(71) Applicant: **BOEHRINGER INGELHEIM INTERNATIONAL GMBH** [DE/DE]; Binger Strasse 173, 55216 Ingelheim am Rhein (DE).

(72) Inventors; and

(71) Applicants *(for US only)*: **COFFMAN, Jonathan** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **GODFREY, Scott A.** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **OROZCO, Raquel** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **FAHRNER, Robert Lee** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **FIADEIRO, Marcus Andre** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **KOTTMEIER, Robert E.** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **MCLAUGHLIN, Joseph K.** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US). **SALM, Jeffrey Richard** [US/US]; c/o VP, IP, Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Road, PO Box 368, Ridgefield, Connecticut 06877 (US).

(74) Agent: **LOCKENOUR, Andrea** et al.; Boehringer Ingelheim Corporation, 900 Ridgebury Road, P.O. Box 368, Ridgefield, Connecticut 06877 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME,

(54) Title: INTEGRATED AND CONTINUOUS RECOMBINANT PROTEIN MANUFACTURING

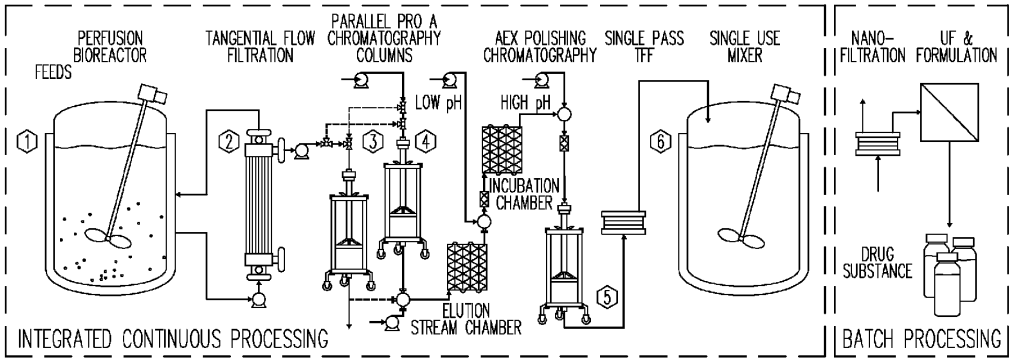


FIG. 6

(57) Abstract: Integrated systems and methods for the manufacturing of recombinant proteins in mammalian cells are provided. The systems and methods include a single-use bioreactor (SUB), a tangential flow filtration system, a column chromatography skid, a tankless hold, a virus inactivation plug flow reactor, and pumps.

[Continued on next page]

WO 2020/205559 A1

MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*